09/546,857 Listing of Claims:

Claims 1-56 (canceled)

Claim ~~57~~ 44 (currently amended): A variant of human VEGF comprising amino acid substitutions D63S, G65M, and L66R, wherein the variant exhibits a higher KDR to Flt-1 binding ratio as compared with native VEGF.

Claim ~~58~~ 45 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim ~~57~~ 44.

Claim ~~59~~ 46 (previously presented): A vector comprising the nucleic acid of claim ~~58~~ 45.

Claim ~~60~~ 1 (currently amended): A variant of human VEGF comprising one or more non-conservative amino acid substitution(s) at residues 63 to 66 and one or more amino acid substitution(s) at residues 18, 21, 22, or 25, wherein the VEGF variant exhibits ~~selective binding affinity for KDR receptor~~ a higher KDR to Flt-1 binding ratio as compared with native VEGF.

Claim ~~61~~ 18 (currently amended): The VEGF variant of claim ~~60~~ 1, wherein at least one of the amino acid substitution(s) comprises D63S, G65M, or L66R.

Claim ~~62~~ 2 (currently amended): The VEGF variant of claim ~~60~~ 1, wherein at least one of the amino acid substitution(s) comprises M18E, Y21L, Q22R, or Y25S.

Claim ~~63~~ 3 (previously presented): The VEGF variant of claim ~~60~~ 1, wherein the amino acid substitutions comprise M18E, Y21L, Q22R, and Y25S.

Claim ~~64~~ 27 (previously presented): The VEGF variant of claim ~~60~~ 1 wherein the amino acid substitutions comprise D63S, G65M, and L66R.

Claim ~~65~~ 28 (currently amended): The VEGF variant of claim ~~64~~ 27, wherein at least one of the amino acid substitution(s) comprise M18E, Y21L, Q22R, or Y25S.

Claim ~~66~~ 19 (currently amended): The VEGF variant of claim ~~6461~~ 18, wherein the amino acid substitutions comprise M18E, Y21L, Q22R, and Y25S.

Claim ~~67~~ 29 (currently amended): ~~A~~The VEGF variant of claim ~~6066~~ 28, comprising ~~one of the following combinations of~~ amino acid substitutions:

~~(a)~~ M18E, D63S, G65M, and L66R;

~~(b) Y21L, D63S, G65M, and L66R;~~

~~(c) Q22R, D63S, G65M, and L66R;~~

~~(d) Y25S, D63S, G65M, and L66R;~~

~~(e) M18E, Y21L, D63S, G65M, and L66R;~~

~~(f) M18E, Q22R, D63S, G65M, and L66R;~~

~~(g) M18E, Y25S, D63S, G65M, and L66R;~~

~~(h) Y21L, Q22R, D63S, G65M, and L66R;~~

~~(i) Y21L, Y25S, D63S, G65M, and L66R;~~

~~(j) Q22R, Y25S, D63S, G65M, and L66R;~~

~~(k) M18E, Y21L, Q22R, D63S, G65M, and L66R;~~

~~(l) M18E, Q22R, Y25S, D63S, G65M, and L66R;~~

~~(m) Y21L, Q22R, Y25S, D63S, G65M, and L66R;~~

~~(n) M18E, Y21L, Q22R, Y25S, and D63S;~~

~~(o) M18E, Y21L, Q22R, Y25S, and G65M;~~

~~(p) M18E, Y21L, Q22R, Y25S, and L66R;~~

~~(q) M18E, Y21L, Q22R, Y25S, D63S, and G65M;~~

~~(r) M18E, Y21L, Q22R, Y25S, D63S, and L66R;~~

~~(s) M18E, Y21L, Q22R, Y25S, G65M, and L66R; or~~

~~(t) M18E, Y21L, Q22R, Y25S, D63S, G65M, and L66R.~~

Claim ~~68~~ 5 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim ~~60~~ 1.

Claim 69 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 63.

Claim 70 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 68.

Claim 71 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 67.

Claim 72 (previously presented): A vector comprising the nucleic acid of claim 68.

Claim 73 (previously presented): A host cell comprising the vector of claim 72.

Claim 74 (previously presented): A composition comprising the VEGF variant of claim 60 and a carrier.

Claim 75 (previously presented): The composition of claim 74, wherein the carrier is a pharmaceutically acceptable carrier.

Claim 76 (previously presented): An assay for detecting KDR receptor, comprising contacting an isolated cell or tissue with a VEGF variant of claim 60 and assaying for binding of the VEGF variant to the cell or tissue.

Claim 77 (previously presented): A method for stimulating phosphorylation of a KDR receptor, comprising contacting a cell with a VEGF variant of claim 60 in amount effective to stimulate phosphorylation of the KDR receptor.

Claim 78 (previously presented): A method for stimulating MAP kinase activation, comprising contacting a cell with a VEGF variant of claim 60 in amount effective to stimulate phosphorylation of MAP kinase.

Claim 13 (previously presented): A method for stimulating PLC-gamma activation, comprising contacting a cell with a VEGF variant of claim 1 in amount effective to stimulate phosphorylation of PLC-gamma.

Claim 14 (previously presented) A method for stimulating PI 3'-kinase activation, comprising contacting a cell with a VEGF variant of claim 1 in amount effective to stimulate phosphorylation of PI 3'-kinase.

Claim 15 (previously presented): A method for stimulating vasculogenesis or angiogenesis, comprising contacting endothelial cells expressing KDR receptor with an effective amount of a VEGF variant of claim 1.

Claim 16 (previously presented): A method for promoting the migration of endothelial cells, comprising contacting endothelial cells expressing KDR receptor with an effective amount of a VEGF variant of claim 1.

Claim 47 (currently amended): A variant of human VEGF comprising two or more amino acid substitutions at residues 17 to 25, wherein the VEGF variant exhibits a higher KDR to Flt-1 binding ratio as compared with native VEGF.

Claim 48 (previously presented): The VEGF variant of claim 47, wherein the amino acid substitutions comprise two or more amino acid substitutions at residues 18, 21, 22, or 25.

Claim 49 (currently amended): The VEGF variant of claim 47, wherein at least one of the amino acid substitution(s) comprise M18E, Y21L, Q22R, or Y25S.

Claim 50 (previously presented): The VEGF variant of claim 47, wherein the amino acid substitutions comprise M18E, Y21L, Q22R, and Y25S.

Claim 87 (previously presented): The VEGF variant of claim 83, wherein the amino acid substitutions comprise F17I, M18E, Y21F, Q22K, and Y25S.

Claim 88 (previously presented): The VEGF variant of claim 83, wherein the amino acid substitutions comprise F17I, M18E, Y21F, Q22E, and Y25I.

Claim 89 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 83.

Claim 90 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 88.

Claim 91 (previously presented): The VEGF variant of claim 60, wherein the amino acid substitutions further comprise a substitution at residue 17.

Claim 92 (currently amended): A variant of human VEGF, comprising:

(a) one or more amino acid substitution(s) at residues 17-25, and

(b) one or more amino acid substitution(s) at residues 63-66;

wherein amino acid residue 60 is cysteine, and the variant exhibits a higher KDR to Flt-1 binding ratio as compared with native VEGF.

Claim 93 (new): The VEGF variant of claim 65, comprising amino acid substitutions Y21L, D63S, G65M, and L66R.

Claim 94 (new): The VEGF variant of claim 65, comprising amino acid substitutions Q22R, D63S, G65M, and L66R.

Claim 95 (new): The VEGF variant of claim 65, comprising amino acid substitutions Y25S, D63S, G65M, and L66R.

Claim 96 (new): The VEGF variant of claim 65, comprising amino acid substitutions M18E, Y21L, D63S, G65M, and L66R.

Claim 36 (new): The VEGF variant of claim 28, comprising amino acid substitutions M18E, Q22R, D63S, G65M, and L66R.

Claim 37 (new): The VEGF variant of claim 28, comprising amino acid substitutions M18E, Y25S, D63S, G65M, and L66R.

Claim 38 (new): The VEGF variant of claim 28, comprising amino acid substitutions Y21L, Q22R, D63S, G65M, and L66R.

Claim 39 (new): The VEGF variant of claim 28, comprising amino acid substitutions Y21L, Y25S, D63S, G65M, and L66R.

Claim 40 (new): The VEGF variant of claim 28, comprising amino acid substitutions Q22R, Y25S, D63S, G65M, and L66R.

Claim 41 (new): The VEGF variant of claim 28, comprising amino acid substitutions M18E, Y21L, Q22R, D63S, G65M, and L66R.

Claim 42 (new): The VEGF variant of claim 28, comprising amino acid substitutions M18E, Q22R, Y25S, D63S, G65M, and L66R.

Claim 43 (new): The VEGF variant of claim 28, comprising amino acid substitutions Y21L, Q22R, Y25S, D63S, G65M, and L66R.

Claim 20 (new): The VEGF variant of claim 19, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, and D63S.

Claim 21 (new): The VEGF variant of claim 19, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, and G65M.

Claim 22 (new): The VEGF variant of claim 19, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, and L66R.

Claim 23 (new): The VEGF variant of claim 19, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, D63S, and G65M.

09/546,857 Listing of Claims:

Claims 1-56 (canceled)

Claim 57 (currently amended): A variant of human VEGF comprising amino acid substitutions D63S, G65M, and L66R, wherein the variant exhibits a higher KDR to Flt-1 binding ratio as compared with native VEGF.

Claim 58 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 57.

Claim 59 (previously presented): A vector comprising the nucleic acid of claim 58.

Claim 60 (currently amended): A variant of human VEGF comprising one or more non-conservative amino acid substitution(s) at residues 63 to 66 and one or more amino acid substitution(s) at residues 18, 21, 22, or 25, wherein the VEGF variant exhibits ~~selective binding affinity for KDR receptor~~ a higher KDR to Flt-1 binding ratio as compared with native VEGF.

Claim 61 (currently amended): The VEGF variant of claim 60, wherein at least one of the amino acid substitution(s) comprises D63S, G65M, or L66R.

Claim 62 (currently amended): The VEGF variant of claim 60, wherein at least one of the amino acid substitution(s) comprises M18E, Y21L, Q22R, or Y25S.

Claim 63 (previously presented): The VEGF variant of claim 60, wherein the amino acid substitutions comprise M18E, Y21L, Q22R, and Y25S.

Claim 64 (previously presented): The VEGF variant of claim 60 wherein the amino acid substitutions comprise D63S, G65M, and L66R.

Claim 65 (currently amended): The VEGF variant of claim 64, wherein at least one of the amino acid substitution(s) comprise M18E, Y21L, Q22R, or Y25S.

Claim 66 (currently amended): The VEGF variant of claim ~~64~~61, wherein the amino acid substitutions comprise M18E, Y21L, Q22R, and Y25S.

Claim 67 (currently amended): ~~A~~The VEGF variant of claim ~~60~~65, comprising ~~one of the following combinations of~~ amino acid substitutions~~:~~

~~(a)~~ M18E, D63S, G65M, and L66R;

~~(b) Y21L, D63S, G65M, and L66R;~~

~~(c) Q22R, D63S, G65M, and L66R;~~

~~(d) Y25S, D63S, G65M, and L66R;~~

~~(e) M18E, Y21L, D63S, G65M, and L66R;~~

~~(f) M18E, Q22R, D63S, G65M, and L66R;~~

~~(g) M18E, Y25S, D63S, G65M, and L66R;~~

~~(h) Y21L, Q22R, D63S, G65M, and L66R;~~

~~(i) Y21L, Y25S, D63S, G65M, and L66R;~~

~~(j) Q22R, Y25S, D63S, G65M, and L66R;~~

~~(k) M18E, Y21L, Q22R, D63S, G65M, and L66R;~~

~~(l) M18E, Q22R, Y25S, D63S, G65M, and L66R;~~

~~(m) Y21L, Q22R, Y25S, D63S, G65M, and L66R;~~

~~(n) M18E, Y21L, Q22R, Y25S, and D63S;~~

~~(o) M18E, Y21L, Q22R, Y25S, and G65M;~~

~~(p) M18E, Y21L, Q22R, Y25S, and L66R;~~

~~(q) M18E, Y21L, Q22R, Y25S, D63S, and G65M;~~

~~(r) M18E, Y21L, Q22R, Y25S, D63S, and L66R;~~

~~(s) M18E, Y21L, Q22R, Y25S, G65M, and L66R; or~~

~~(t) M18E, Y21L, Q22R, Y25S, D63S, G65M, and L66R.~~

Claim 68 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 60.

Claim 69 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 63.

Claim 70 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 65.

Claim 71 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 67.

Claim 72 (previously presented): A vector comprising the nucleic acid of claim 68.

Claim 73 (previously presented): A host cell comprising the vector of claim 72.

Claim 74 (previously presented): A composition comprising the VEGF variant of claim 60 and a carrier.

Claim 75 (previously presented): The composition of claim 74, wherein the carrier is a pharmaceutically acceptable carrier.

Claim 76 (previously presented): An assay for detecting KDR receptor, comprising contacting an isolated cell or tissue with a VEGF variant of claim 60 and assaying for binding of the VEGF variant to the cell or tissue.

Claim 77 (previously presented): A method for stimulating phosphorylation of a KDR receptor, comprising contacting a cell with a VEGF variant of claim 60 in amount effective to stimulate phosphorylation of the KDR receptor.

Claim 78 (previously presented): A method for stimulating MAP kinase activation, comprising contacting a cell with a VEGF variant of claim 60 in amount effective to stimulate phosphorylation of MAP kinase.

Claim 79 (previously presented): A method for stimulating PLC-gamma activation, comprising contacting a cell with a VEGF variant of claim 60 in amount effective to stimulate phosphorylation of PLC-gamma.

Claim 80 (previously presented) A method for stimulating PI 3'-kinase activation, comprising contacting a cell with a VEGF variant of claim 60 in amount effective to stimulate phosphorylation of PI 3'-kinase.

Claim 81 (previously presented): A method for stimulating vasculogenesis or angiogenesis, comprising contacting endothelial cells expressing KDR receptor with an effective amount of a VEGF variant of claim 60.

Claim 82 (previously presented): A method for promoting the migration of endothelial cells, comprising contacting endothelial cells expressing KDR receptor with an effective amount of a VEGF variant of claim 60.

Claim 83 (currently amended): A variant of human VEGF comprising two or more amino acid substitutions at residues 17 to 25, wherein the VEGF variant exhibits a higher KDR to Flt-1 binding ratio as compared with native VEGF.

Claim 84 (previously presented): The VEGF variant of claim 83, wherein the amino acid substitutions comprise two or more amino acid substitutions at residues 18, 21, 22, or 25.

Claim 85 (currently amended): The VEGF variant of claim 83, wherein at least one of the amino acid substitution(s) comprise M18E, Y21L, Q22R, or Y25S.

Claim 86 (previously presented): The VEGF variant of claim 83, wherein the amino acid substitutions comprise M18E, Y21L, Q22R, and Y25S.

Claim 87 (previously presented): The VEGF variant of claim 83, wherein the amino acid substitutions comprise F17I, M18E, Y21F, Q22K, and Y25S.

Claim 88 (previously presented): The VEGF variant of claim 83, wherein the amino acid substitutions comprise F17I, M18E, Y21F, Q22E, and Y25I.

Claim 89 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 83.

Claim 90 (previously presented): An isolated nucleic acid sequence encoding the VEGF variant of claim 86.

Claim 91 (previously presented): The VEGF variant of claim 60, wherein the amino acid substitutions further comprise a substitution at residue 17.

Claim 92 (currently amended): A variant of human VEGF, comprising:

(a) one or more amino acid substitution(s) at residues 17-25, and

(b) one or more amino acid substitution(s) at residues 63-66;

wherein amino acid residue 60 is cysteine, and the variant exhibits a higher KDR to Flt-1 binding ratio as compared with native VEGF.

Claim 93 (new): The VEGF variant of claim 65, comprising amino acid substitutions Y21L, D63S, G65M, and L66R.

Claim 94 (new): The VEGF variant of claim 65, comprising amino acid substitutions Q22R, D63S, G65M, and L66R.

Claim 95 (new): The VEGF variant of claim 65, comprising amino acid substitutions Y25S, D63S, G65M, and L66R.

Claim 96 (new): The VEGF variant of claim 65, comprising amino acid substitutions M18E, Y21L, D63S, G65M, and L66R.

Claim 97 (new): The VEGF variant of claim 65, comprising amino acid substitutions M18E, Q22R, D63S, G65M, and L66R.

Claim 98 (new): The VEGF variant of claim 65, comprising amino acid substitutions M18E, Y25S, D63S, G65M, and L66R.

Claim 99 (new): The VEGF variant of claim 65, comprising amino acid substitutions Y21L, Q22R, D63S, G65M, and L66R.

Claim 100 (new): The VEGF variant of claim 65, comprising amino acid substitutions Y21L, Y25S, D63S, G65M, and L66R.

Claim 101 (new): The VEGF variant of claim 65, comprising amino acid substitutions Q22R, Y25S, D63S, G65M, and L66R.

Claim 102 (new): The VEGF variant of claim 65, comprising amino acid substitutions M18E, Y21L, Q22R, D63S, G65M, and L66R.

Claim 103 (new): The VEGF variant of claim 65, comprising amino acid substitutions M18E, Q22R, Y25S, D63S, G65M, and L66R.

Claim 104 (new): The VEGF variant of claim 65, comprising amino acid substitutions Y21L, Q22R, Y25S, D63S, G65M, and L66R.

Claim 105 (new): The VEGF variant of claim 66, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, and D63S.

Claim 106 (new): The VEGF variant of claim 66, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, and G65M.

Claim 107 (new): The VEGF variant of claim 66, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, and L66R.

Claim 108 (new): The VEGF variant of claim 66, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, D63S, and G65M.

Claim 109 (new): The VEGF variant of claim 66, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, D63S, and L66R.

Claim 110 (new): The VEGF variant of claim 66, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, G65M, and L66R.

Claim 111 (new): The VEGF variant of claim 66, comprising amino acid substitutions M18E, Y21L, Q22R, Y25S, D63S, G65M, and L66R.

Requested 3/24/05

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Message: Please deliver to Examiner Spector. Draft claims attached. We have no objections to the proposed reasons for allowance. How do we take care of an extra claims fee, if any?